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PROCESS FOR CORRECTION OF A DISULFIDE MISFOLD IN Fc MOLECULES

Abstract

The present invention concerns a process by which a misfold in an Fc fusion molecule can be prevented or corrected. In one embodiment, the process comprises (a) preparing a pharmacologically active compound comprising an Fc domain; (b) treating the fusion molecule with a copper (II) halide; and (c) isolating the treated fusion molecule. The pharmacologically active compound can be an antibody or a fusion molecule comprising a pharmacologically active domain and an Fc domain. The preferred copper (II) halide is $CuCl_2$. The preferred concentration thereof is at least about 10 mM for fusion molecules prepared in E. coli; at least about 30 mM for fusion molecules prepared in CHO cells. The process can be employed with any number of pharmacologically active domains. Preferred pharmacologically active domains include OPG proteins, leptin proteins, soluble portions of TNF receptors (e.g., wherein the fusion molecule is etanercept), IL-1ra proteins, and TPO-mimetic peptides. The Fc domain preferably has a human sequence, with an Fc sequence derived from IgG1 most preferred. An exemplary Fc sequence is shown in Figure 5 hereinafter.